PATENT COOPERATION TREATY

REC'D 14 JUN 2005
WIPO PCT

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

4/8

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below
International application No. PCT/EP2005/050206	International filing date *(day/month/year)* 19.01.2005
Priority date *(day/month/year)* 22.01.2004	
International Patent Classification (IPC) or both national classification and IPC C07D239/42, C07D409/14, C07D403/04, C07D405/04, A61K31/505, A61K31/506, A61P35/00, A61P37/00	
Applicant ALTANA PHARMA AG	

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Traegler-Goeldel, M

Telephone No. +49 89 2399-8278

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/050206

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/050206

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 25, 28, 29, 32,33

because:

☒ the said international application, or the said claims Nos. 25, 28, 29, 32, 33 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-33
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-33
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-24, 26, 27, 30, 31
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

see form 210

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

re item III:

Claims 25, 28, 29, 32 and 33 have to be considered as being directed to the treatment of the human and/or animal body. Under the terms of Rule 67.1 and Art. 34 (4)a)i) PCT the International Preliminary Examination Authority is not required to carry out an examination on such claims.

re item V:

1. Prior art

a, The examining procedure is based on the documents cited in the International Search Report:

D1: WO 2005/026129 A1 (AXXIMA PHARMACEUTICALS AG, GERMANY) 24 March 2005 (2005-03-24)
D2: US-A-5 821 246 (BROWN ET AL) 13 October 1998 (1998-10-13)
D3: WO 99/24440 A (PFIZER PRODUCTS INC; MUNCHHOF, MICHAEL, JOHN; SOBOLOV-JAYNES, SUSAN, B) 20 May 1999 (1999-05-20)

b, **The Applicant is explicitly asked to give a detailed explanation** with respect to the disclaimers in the claims, i.e. from which documents these compounds are known and were exactly they are to be found. In this context it is brought to the Applicant's attention, that if the reason for the disclaimer were to be seen in a document disclosing compounds showing the same or related activities as the present compounds, this or these documents were to be considered relevant for the assessment of novelty and inventive step and have to be cited as relevant prior art in the description.

2. Novelty

The claimed 6-(hetero)aryl-4-(4-(hetero)arylsulfonylaminophenyl)aminopyrimidine derivatives are considered to be novel with respect to documents D2 to D3 due to the monocyclic pyrimidine residue instead of the condensed pyrimidines according to D2

(quinazolines) and D3 (thienopyrimidines). Thus the subject matter of claims 1 to 33 is considered to fulfil the requirements of Art. 33 (2) PCT with respect to the cited prior art.

3. Inventive step

Relevant close prior art is to be seen in documents D2 and D3, disclosing 4-phenylaminoquinazoline and 4-(hetero)arylaminothienopyrimidine derivatives that are potent kinase inhibitors as are the present 6-(hetero)aryl-4-(hetero)arylsulfonylamino-phenyl)aminopyrimidine derivatives of the present application. Therefore, documents D2 and D3 are considered to represent the closest prior art concerning the alleged activity.

If the problem underlying the present application were to be seen in provision of further compounds that may be used as kinase inhibitors, the solution of this problem can in principal (see item 1b above) be considered as being inventive for the following reasons:

The teaching of documents D2 and D3 is clearly that an essential feature of all compounds disclosed therein is the condensed pyrimidine residue, i.e it is an essential feature for the alleged activity and that either the amino residue in position 4 or the substituents of the phenylamino residue in position 4 may be varied to a great extent. From the very many compounds explicitly disclosed in these documents only two compounds are disclosed in D2 and only one compound is disclosed in D3 bearing a phenylsulfonylamino substituent in the phenyl residue of the phenylamino residue in position 4 of the condensed pyrimidine as obligatory in the present uncondensed pyrimidine derivatives. Therefore, these documents, neither taken alone or in combination, would have taught the skilled person to replace the condensed pyrimidine as known from the prior art to be essential by the monocyclic pyrimidine residue and furthermore to select from the many possible substituents of the (potential, D2) phenylamino moiety in position 4 exactly the 4-(hetero)arylsulfonylamino residue. As can be seen from the examples and the test results as given in the description, the above mentioned problem has obviously been solved by the compounds of present claim 1. Therefore, presumed there is no more prior art document disclosing any 6-(hetero)aryl-4-(4-(hetero)arylsulfonylaminophenyl)-aminopyrimidine derivatives (see item 1b above) and only then, the present application

appears to fulfil the requirements of Art.33 (3) PCT, with respect to the cited prior art.

4. Industrial applicability

No objection arises with respect to claims 1-24, 26, 27, 30 and 31, since the claimed compounds may be used for the production of pharmaceutical compositions.

re item VI:

It is brought to the Applicant's attention, that the part of document D1 as cited above and entitled to its EP priority, if entering the European phase were relevant for the consideration of novelty and inventive step.

re item VIII:

It appears that claims 30, 31, 32 and 33 are identical with the corresponding parts of claims 26, 27, 28 and 29, i.e. with respect to the last 9 compounds of claim 26.